Fetal Brain Injury: The Effects and Detection of Asphyxia, and The Consequences of Isohydric Hypoxia.

Adamsons, K., Arnold, S.

During the last decade, our knowledge has advanced substantially regarding the various states of oxygen deprivation that can confront the fetus during the antepartum period and during labor.

Experimental models using the pregnant Rhesus monkey have been particularly useful in elucidating the complex relationships between the various forms of impaired oxygenation, their physiologic manifestations, and their immediate and long term sequelae.

The main concept that has emerged is that distinct types of brain damage result from different forms of fetal oxygen deprivation, and that total intra-partum asphyxia causes a type of brain pathology rarely observed in the human infant.

In the clinical setting, there are three principal forms of fetal oxygen deprivation: a) total asphyxia, denoting a complete cessation of gaseous exchange between mother and fetus, b) partial prolonged asphyxia, characterized by hypoxia, hypercarbia and acidosis, and c) isohydric hypoxia (=indolent hypoxia), reflecting a low fetal P_{O_2} in the presence of normal or near normal P_{CO_2} and pH.

The initial animal studies examined the effects of abrupt total or partial but prolonged asphyxia upon the fetus. Distinct forms of grey matter injury were produced, which involved depending on the rate of development, the degree of asphyxia and tissue carbohydrate stores, the brain stem nuclei or the cortical regions. The physiologic responses of the fetus during these periods of asphyxia have been extensively studied, and have provided the theoretic basis for the interpretation of antepartum and intrapartum fetal heart rate monitoring.

Diagnosis of acute total asphyxia, as it may occur with cardiac arrest, severe maternal hypotension and cord occlusion, rarely presents a problem as the clinical signs are obvious. The fetal heart rate shows an abrupt decline during the initial 80-90 seconds at which time the arterial PO_2 declines to 7-8 torr; thereafter, the heart rate remains essentially constant until cardiac arrest.

In contrast, the signs of partial prolonged asphyxia, which occurs chiefly during labor as result of maternal hypotension, partial placental separation, partial cord occlusion, and excessive concentration of endogenous or exogenous cathecolamines, are more subtle. If the existance of these conditions is recognized, the degree of fetal asphyxia can be determined by analysis of fetal capillary blood. If blood sampling is not possible, fetal heart rate as obtained by continuous monitoring can be resorted to as an indicator of fetal oxygenation. The main physiologic expression of the asphyxial state is a periodic fall in fetal heart rate secondary to further reduction of fetal PO_2 brought about by uterine contractions. In the presence of normal uterine contractions, the phenomenon of "late decelerations" will occur when fetal arterial

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PO_2 falls below 20 torr. Thus, in the absence of uterine contractions, fetal heart rate and ECG will remain essentially unaffected in spite of considerable reduction in oxygen supply. A rather accurate estimation of fetal O_2 stores in the absence of labor can be obtained with intermittent injections of oxytocin in increasing doses until contractions of sufficient length are achieved to produce "late decelerations". The O_2 concentration of fetal blood prior to the induced contraction can be then calculated from the knowledge of fetal oxygen consumption (5ml/kg.min), and the fact that fetal heart rate begins to decline when O_2 concentration in fetal blood falls below 5 ml/100ml. This test is called component analysis of induced "late deceleration", and has been developed from data from experiments in the pregnant Rhesus monkey exposed to partial asphyxia. Other indicators of partial fetal asphyxia are: tachycardia, and reduction or loss of reflexly mediated changes in fetal heart rate ("beat to beat variability"). However, present knowledge does not permit the use of these indicators to quantitate the impairment of oxygenation, or to relate them to the development of brain injury.

The nearly routine use of intra-partum fetal monitoring as is the practice in many hospitals, has markedly reduced the incidence of clinically significant degrees of asphyxia during labor, and thus the occurance of cortical grey matter injury. Seizure disorders of the newborn, secondary to intrapartum deprivation of oxygen have become, in fact, a rarety.

White matter injury, in contrast, has been diagnosed with increasing frequency chiefly among pre-term newborns maintained on artificial ventilation. The etiology of this pattern of brain injury which was thought to be pathognomonic to prematurity, has remained uncertain.

Recently, white matter injury has been produced experimentally in animals by exposure to prolonged periods of normocarbic hypoxia. White matter has a lower capillary density than grey matter. In the presence of normocarbic hypoxia, there will be little or no compensatory vasodilation, and tissues with fixed oxygen requirements and sparse blood supply will be most severely affected.

Cerebral white matter damage from hypoxia varies from destruction of restricted foci in the periventricular white matter to complete desolution of white matter throughout the hemispheres, and, sometimes the brain stem. While multicystic leukoencephalopathy has been observed not infrequently in preterm infants ventilated by artificial means, the incidence of periventricular leukomalacia in term newborns with no apparent exposure to antepartum asphyxia is still unknown. As the index of suspicion of this form of brain injury increases, and as our diagnostic modalities improve, white matter injury might prove to be the more prevalant form of antepartum brain injury.

Infants prone to this form of brain damage are those exposed in utero to prolonged periods of partial reduction of oxygenation with relatively normal pH and P_{CO_2}. These fetuses may tolerate normal labor without expressing any typical signs of distress; their course

in the newborn nursery is also likely to be benign. Neurologic abnormalities, which may vary from mild strabismus or slight spastic diplagia to severe dementia associated with quadriplegia are likely to be manifested only during the first or second year of post-natal life.

Isohydric hypoxia can occur in the presence of severe fetal anemia, carbon monoxide poisoning, and under conditions of impaired unbilical circulation (e.g. fetal hyperinsulinemia, congenital syphilis, Van Gierkie's disease, and non-patency of foramen ovale). Other disorders include partial placental separation, reduction of fetal cardiac output by beta adrenergic blockade or antihypertensive therapy, and over stimulation of maternal sympathetic system.

There are no tests presently available that could detect with precision the presence of isohydric hypoxia of the fetus, because in this condition, fetal heart rate is even a less sensitive indicator of impaired oxygenation than in the presence of partial asphyxia. If isohydric hypoxia is suspected, the evaluation of fetal behavior (e.g. movements, "breathing" and swallowing) might provide an estimate of the degree of hypoxia. This has been shown to be the case with anemic fetuses.

In conclusion, continuous intrapartum fetal heart rate monitoring combined with analysis of fetal blood have been highly successful in detecting fetal asphyxia before it becomes permanently injurious to the grey matter.

In contrast, our ability to detect and to quantitate isohydric hypoxia during the ante-partum course has remained nominal. Because of the importance of this condition as an etiologic factor of neurolocig abnormalities in infants and children, further developments in this field should be of considerable clinical merit.

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Prof.Dr.K.Adamsons
University of Puerto Rico
Medical Sciences Campus
Dept.of Obstet. & Gynecology
G.P.O.Box 5067
USA-San Juan, Puerto Rico 00936